UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/501,682	02/02/2005	Paul G Shiels	0380-P03437US0	4505

110 7590 07/25/2006

DANN, DORFMAN, HERRELL & SKILLMAN
1601 MARKET STREET
SUITE 2400
PHILADELPHIA, PA 19103-2307

EXAMINER	
LIETO, LOUIS D	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 07/25/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/501,682	SHIELS, PAUL G	
	Examiner	Art Unit	
	Louis D. Lieto	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22 and 24-35* is/are pending in the application.

4a) Of the above claim(s) *1-17,20-32 and 34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18,19 and 33-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response to the Restriction requirement was received on 5/02/2006. Claims 1-22, 24-35 are pending in the instant application. Applicant's election with traverse of Group VI, claims 18,19,33-35, drawn to a method of treatment of donor tissues to reduce the risk of rejection comprising treating the tissue with an agent to modulate the activity, half-life or expression and optionally, the effective functionality of at least the G22P1 telomerase binding protein, further comprising treating the tissue with an agent to prevent tissue senescence or cell death, is acknowledged.

Claims 1-17, and 20-32 and 34 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 5/02/2006.

Response to Arguments

Applicant's election with traverse of Group I in the reply filed on 5/02/2006 is acknowledged. Applicant argues that the restriction requirement is improper because the examiner has failed to comply with the relevant portions of the MPEP pertaining to lack of unity of invention. This is not found to be persuasive. Applicant argues that since a finding of lack of unity of invention was not found during examination of the PCT then it is improper to make such a finding in the examination of the national stage. This is not found to be persuasive, since the examination of the PCT and the national stage are made independently of one another. Applicant also argues that it was improper for the examiner to restrict the invention to a single telomerase

protein. However, each listed protein has a patentably distinct structure and function from the other proteins and there is no indication that any of the listed proteins can be substituted for the other. Therefore restriction is proper. Applicant is reminded that the instant application was submitted under 35 U.S.C. 371. Therefore PCT Rule 13.1 and 13.2 will be followed when considering unity of invention of claims of different categories.

An international application should relate to only one invention or, if there is more than one invention, the inclusion of those inventions in one international application is only permitted if all inventions are so linked as to form a single general inventive concept (PCT Rule 13.1). With respect to a group of inventions claimed in an international application, unity of invention exists only when there is a technical relationship among the claimed inventions involving one or more of the same or corresponding special technical features. The expression "special technical features" is defined in PCT Rule 13.2 as meaning those technical features that define a contribution which each of the inventions, considered as a whole, makes over the prior art. The determination is made on the contents of the claims as interpreted in light of the description and drawings (if any).

Whether or not any particular technical feature makes a "contribution" over the prior art, and therefore constitutes a "special technical feature," should be considered with respect to novelty and inventive step. For example, a document discovered in the international search shows that there is a presumption of lack of novelty or inventive step in a main claim, so that there may be no technical relationship left over the prior art among the claimed inventions involving one or more of the same or corresponding special technical features, leaving two or more dependent claims without a single general inventive concept. See MPEP 1850

Further, the applicant has not traversed the basis of the examiner's determination that the unity of the claimed inventions was broken by the cited prior art. As previously stated:

Since the claimed subject matter was known from the prior art document of GB 2321642 A the subject matters of claims 1-22, 24-35 are not so linked as to form a single general inventive concept (Rule 13.1 PCT) as they appear not to be linked by a new and inventive common special technical feature in the sense of Rule 13.2 PCT by taking into account the state of the art.

Applicant has not presented any arguments traversing the grounds of rejection based on the lack of a unifying special technical feature amongst the claimed inventions. Therefore restriction is appropriate.

The requirement is still deemed proper and is therefore made FINAL.

Claims 18,19,33 and 35 are under consideration.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Sequence Compliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2), see for example page 18 , which disclose numerous sequences without assigned numbers. Sequences appearing in the specification must be identified by sequence identifier in accordance with 37 C.F.R. 1.821(d). Specifically, the sequences on page 18 require sequence identifiers. This application clearly fails to comply with requirements of 37 C.F.R 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published in the *Federal Register* at 65 FR 54604 (September 8, 2000) and 1238 OG 145 (September 19, 2000). Applicant must provide an initial computer readable form (CRF) copy of the "Sequence Listing", an initial paper copy or compact disc copy of the "Sequence Listing", as well as an amendment directing its entry into application. Applicant must also provide a statement that the content of the sequence listing information recorded in computer readable format is identical to the written (on paper or compact disc) sequence listing and, where applicable, includes no new matter, as required by 37 C.F.R. 1.821 (e), 1.821 (f), 1.821 (g), 1.825 (b), 1.825 (d). If applicant desires the sequence listing in the instant application to be identical with that of another application on file in the

Patent and Trademark Office, such request in accordance with 37 C.F.R. 1.821(e) may be submitted in lieu of a new CRF.

For the response to this office action to be complete the applicant is required to comply with the Requirements for Patent Applications Containing Nucleotide Sequence and/or amino acid sequence disclosures.

Claim Objections

Claims 18,19, 33 and 35 are objected to because of the following informalities: The claims depend from withdrawn claim 15. For the purposes of compact prosecution the limitations of withdrawn claim 15, consistent with the subject matter under examination, will be read into the claims under consideration. However, it is noted that claim 15 has been withdrawn from examination. Appropriate correction is required.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. Examples of embedded hyperlinks are present on page3, lines 28-35 and page 5, line 9.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 18, 19 and 33 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a method of treatment of donor tissues to reduce the risk of rejection comprising treating the tissue with an agent to modulate the activity, half-life or expression and optionally, the effective functionality of at least the G22P1 telomerase binding protein or any homologues or analogues thereof, further comprising treating the tissue with an agent to prevent tissue senescence or cell death. The claims encompass a genus of proteins that are defined solely by the fact that they are homologues or analogues of the G22P1 protein.

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing characteristics of the genus. While the specification contemplates modulating the activity, half-life or expression and optionally, the effective functionality of at least the G22P1 telomerase binding protein or any homologues or analogues thereof, it does not provide any defining characteristics of the homologues or analogues of the G22P1 protein (Specification pg. 4, line 32-pg. 5 line 9).

The factors to be considered when assessing possession of the claimed invention include disclosure of complete or partial structure, physical and/ or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any

combination thereof. In regards to the genus of homologues or analogues of the G22P1 protein, there is no requirement in the claims or the specification that these homologues or analogues retain any particular structural or functional characteristics of the wild-type G22P1 protein. The specification does not contemplate that the claimed homologues or analogues must have any conserved functional domains or structural features in order to be used in the claimed method.

Accordingly, in the absence of sufficient recitation of a distinguishing identifying characteristic, the specification does not provide adequate written description of the claimed genus of proteins that are defined solely by the fact that they are homologues or analogues of the G22P1 protein.

Further, the claims are drawn to a method of treatment of donor tissues to reduce the risk of rejection comprising treating the tissue with an agent to modulate the activity, half-life or expression and optionally, the effective functionality of at least the G22P1 telomerase binding protein or any homologues or analogues thereof. Wherein the agent to prevent tissue senescence is a calcineurin inhibitor or an analogue thereof. The claims encompass a genus of analogues of any calcineurin inhibitor.

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing characteristics of the genus. The specification contemplates a genus of analogues of any calcineurin inhibitors, but does not provide any guidance on the characteristics of said analogues (Specification pg. 5, line 30-pg. 6 line 7).

The factors to be considered when assessing possession of the claimed invention include disclosure of complete or partial structure, physical and/ or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any

combination thereof. In regards to the genus of analogues of any calcineurin inhibitors, there is no requirement in the claims or the specification that these homologues or analogues retain any particular structural or functional characteristics of any calcineurin inhibitor. The specification does not contemplate that the claimed analogues must have any conserved functional domains or structural features in order to be used in the claimed method.

Accordingly, in the absence of sufficient recitation of a distinguishing identifying characteristic, the specification does not provide adequate written description of the claimed genus of agents defined solely by the fact that they are analogues of a calcineurin inhibitor.

The Revised Interim Guidelines state, "when there is substantial variation with the genus, one must describe a sufficient variety of species to reflect the variation within the genus. In an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus" (Column 2, page 71436, or the Revised Interim Guidelines for Written Description). Case law concurs, stating, "simply describing large genus of compounds is not sufficient to satisfy written description requirement as to particular species or sub-genus" *Fujikawa v. Wattanasin*, 39 USPQ2d 1895 (CA FC 1996). Furthermore, *Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is claimed." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116). Thus, the specification does not meet the written description provision of 35 U.S.C. 112, first paragraph, for a genus of proteins that are defined solely by the fact that they

are homologues or analogues of the G22P1 protein, or a genus of agents defined solely by the fact that they are analogues of any calcineurin inhibitor. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision.

Claims 18,19,33 and 35 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicants claims are drawn to a method of treatment of donor tissues to reduce the risk of rejection comprising treating the tissue with any agent to modulate the activity, half-life or expression and optionally, the effective functionality of at least the G22P1 telomerase binding protein, homologues or analogues, further comprising treating the tissue with an agent to prevent tissue senescence or cell death. Wherein the to prevent tissue senescence agent may be a calcineurin or analogue thereof.

The specification states that an increase in expression of G22P1 expression is indicative of a predisposition to rejection (Specification pg. 4, lines 1-7). Therefore, the disclosure suggests that only decreasing the activity, half-life or expression and optionally, the effective functionality of G22P1 would lead to a reduction in the risk of rejection of any donor tissue. However, Lee et al teaches that treating cells with an agent that decreases the levels of Ku70 (G22P1) induces apoptosis in the cells because of translocation of Bax from the cytosol to the mitochondria {Lee et al. (2005) Carcinogenesis 26:1716-1730;Abstract; pg. 1723, Fig.4}. Increasing the amount of

cell death due to apoptosis in a donor tissue is only likely to increase the risk of rejection. Further, the specification does not provide any guidance demonstrating that modulating the activity, half-life or expression and optionally, the effective functionality of G22P1, homologues or analogues thereof has any effect on the risk of tissue rejection. It is noted that the specification does not provide any guidance as to determine what defines a homologue or analogue of G22P1. Therefore the skilled practitioner would be reduced to guessing as to whether a DNA binding protein was a homologue or analogue of G22P1. The specification provides working examples describing the changes in levels of G22P1 in kidney cells and correlating them with the development of chronic allograft nephropathy (CAN) in kidney transplants (pg. 20, Example 1). However the specification does not provide any guidance that modulating the activity, half-life or expression and optionally, the effective functionality of a marker, such as G22P1, has any effect on the development of CAN in kidneys or the risk of rejection for any other donor tissue.

The art of record teaches that the risks associated with CAN mediated rejection of kidney transplants is associated with the appearance of replicative senescence {Ferlicot et al. (2003) Hum Pathol 34:924-928; Abstract}. However, the distinguishing characteristic and driving force behind replicative senescent cells is the decrease in telomere length below the average telomere length of non-senescent cells (pg. 927, col. 1). Neither the art of record nor the specification provides guidance that modulating the activity, half-life or expression and optionally, the effective functionality of G22P1 has any effect on telomere length. G22P1 is a helicase, without any known ability to act as a telomerase, and thus is without ability to increase the length of the telomeres. Therefore while the specification provides evidence suggesting that changes in levels of G22P1 in kidney cells correlates with the development of CAN in kidney transplants, there is

no evidence provided indicating that G22P1 serves any purpose other than as a possible diagnostic marker of replicative senescence. Finally, neither the specification nor the art of record provide any guidance on any agent that can modulate the activity, half-life or expression and optionally, the effective functionality of G22P1 in order to decrease risk of tissue rejection of any donor transplant. Given the complete lack of guidance in the specification, the skilled practitioner would be reduced to guessing as to what agent could be used to modulate G22P1 in order to decrease risk of donor tissue rejection. Therefore, given the complete lack of guidance in the specification and the art of record, the skilled practitioner would be unable to predict how to practice the invention as claimed, without undue and extensive experimentation.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 18,19,33 and 35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

For the purposes of compact prosecution the limitations of withdrawn claim 15, consistent with the subject matter under examination, will be read into the claims under consideration. Regarding claims 18,19,33-35, the phrase "and optionally" in withdrawn base claim 15 renders the claims indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

No claims allowed.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Lou Lieto whose telephone number is (571) 272-2932. The examiner can normally be reached on Monday-Friday, 9am-5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Patent applicants with problems or questions regarding electronic images that can be viewed in the PAIR can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Dr. Louis D. Lieto
Patent Examiner
Art Unit 1632

Deborah Crouch

DEBORAH CROUCH
PRIMARY EXAMINER
GROUP ~~1800~~ 1630